meters (nm) and a reference wavelength of 610 nm. The concentration of nitrite was determined from a standard curve using dilutions of a stock sodium nitrite solution (200 μM). Samples were tested in triplicate and reported as the mean concentration ±SEM.

The cells from the arthritic animals (SCW Inj., FIG. 6A) produced a significantly greater amount of nitrite in comparison to cells from the control animals. Both experimental and control cell populations showed an increase in nitrite production as the concentration of SCW was increased in the culture medium. The cells obtained from untreated animals and treated with SCW (SCW) in culture also produced significantly greater amounts of nitrite as compared to cells obtained from untreated animals and not treated with SCW (Control, FIG. 7A). The cells from the arthritic animals and the cells from the control animals also demonstrated a significant reduction in nitrite production upon NMMA addition.

The cells obtained from untreated animals and treated with SCW and either canaline (SCW+Canaline, FIG. 7A), canavanine (SCW+Canavanine, FIG. 7B), NAME (SCW+NAME, FIG. 7B), or aminoguanidine (500 or 100 μM Aminoguanidine SCW, FIG. 7C) in culture produced substantially reduced levels of nitrites compared to cells obtained from untreated animals and treated with SCW alone (SCW, FIGS. 7A–C).

EXAMPLE 6

This example demonstrates that cytokines, such as the transforming growth factor-β (TGF-β) and IL-4, reduce inflammation in vivo.

Female Lewis rats received a single dose of SCW on day 0 as described in Example 1. Groups of these animals were given intraperitoneal injections of either 0.1 μg (▼, FIG. 8), 1.0 μg (■, FIG. 8), or 5.0 μg (▲, FIG. 8) of TGF-β (Celtrix) daily beginning on day 0 or no TGF-β (o, FIG. 8). All of the TGF-β-treated arthritic animals showed significantly lower articular indices than untreated arthritic animals.

Some groups of arthritic rats were treated twice a day with 100 ng injections of IL-4 (Schering-Plough, SCW+IL-4, o, FIG. 9). Animals that were treated with SCW and IL-4 showed significant reduction in their articular indices, particularly in chronic inflammation, as compared to animals that were not treated with IL-4 (SCW alone, ●, FIG. 10).

The effectiveness of IL-10, IL-4, and TGF-β in reducing nitrite levels in comparison to control cells, both SCW-stimulated and unstimulated, is shown graphically in FIG. 10.

EXAMPLE 7

This example demonstrates that cytokines, such as the transforming growth factors β1, 2, and 3 (TGF-β1, 2, 3), inhibit the induction of NOS in vitro.

Peripheral blood leukocytes from arthritic female Lewis rats, which were obtained in accordance with Example 1, were grown in DMEM supplemented with SCW as described in Example 5. NMMA (500 μM, Calbiochem), TGF-β1 (10 ng/ml, FIG. 11, Cetrix Pharmaceuticals), or nothing (Control, FIG. 1) was added to each culture. After about 48 hours, aliquots of the culture supernatants were tested for nitrite levels by Griess reaction as described in Example 5. The cytokine TGF-β substantially reduced nitrite production by peripheral blood leukocytes in vitro.

EXAMPLE 8

This example demonstrates that cytokines, such as interleukin 10 (IL-10), reduce nitrite levels in vitro.

Peripheral blood leukocytes were grown in DMEM culture medium supplemented with SCW as described in Example 5. IL-10 (1,000 units, Genzyme) was added to some of the cultures. Treatment with IL-10 resulted in depletion of nitrites produced by the peripheral blood leukocytes (SCW+IL-10, FIG. 12) compared to SCW-treated peripheral blood leukocytes that were not treated with IL-10 (SCW, FIG. 12).

EXAMPLE 9

This example demonstrates that NO scavengers, such as hemoglobin, reduce inflammation in vivo.

Female Lewis rats received SCW on day 0 as described in Example 1. Some of these animals were also injected with 20 mg of hemoglobin (SCW+Hb). Other animals were left untreated (SCW). The articular indices of these animals were determined as described in Example 3. Hemoglobin reduced the articular index of arthritic animals.

EXAMPLE 10

This example demonstrates that NO scavengers, such as hemoglobin, reduce nitrite levels in vitro.

About 4×10^6 rat spleen cells were cultured in DMEM with 5 μg/ml SCW as described in Example 5. The spleen cells were cultured in the absence (**0**, FIG. **13**) or presence of either 2 μM or 10 μM hemoglobin (**2** or **10**, FIG. **13**, Sigma, Biopure, or Somatogen). After about 48 hours, aliquots of the culture supernatants were tested for nitrite levels by Griess reaction as described in Example 5. Cells treated with hemoglobin (**2** or **10**, FIG. **13**) had reduced nitrite levels as compared to untreated control cells (**0**, FIG. **13**).

EXAMPLE 11

This example demonstrates that inhibitors of tetrahydrobiopterin synthesis, such as 2,4-diamino-6-hydroxypyrimidine, reduce nitrite levels in vitro.

Peripheral blood leukocytes from control rats were grown in DMEM culture media in the absence (Control) or presence of 2 μg/ml SCW (SCW) and 5 mM 2,4-diamino-6-hydroxy-pyrimidine (DAHP+SCW, Sigma) (see FIG. **14**). After 48 hours, aliquots of the culture supernatants were tested for nitrite levels by Griess reaction as described in Example 5. Cells treated with 2,4-diamino-6-hydroxy-pyrimidine had reduced nitrite levels as compared to untreated control cells.

All publications, patents, and patent applications cited herein are hereby incorporated by reference to the same extent as if each individual document were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

While this invention has been described with emphasis upon preferred embodiments, it will be obvious to those of ordinary skill in the art that the preferred embodiments may be varied. It is intended that the invention may be practiced otherwise than as specifically described herein. Accordingly, this invention includes all modifications encompassed within the spirit and scope of the appended claims.

What is claimed is:

1. A method for treating a mammal having a chronic inflammatory condition comprising administering an effective amount of a compound selected from the